

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/IB2004/003373

International filing date (day/month/year)
04.10.2004

Priority date (day/month/year)
02.10.2003

International Patent Classification (IPC) or both national classification and IPC
A61K39/095, A61K39/102, A61K39/09

Applicant
CHIRON SRL

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IB2004/003373

300 514 424

AP23 (Revised) 04 APR 2005

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☒ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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INTERNATIONAL SEARCHING AUTHORITY**

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 17 with respect to industrial applicability

because:

- ☒ the said international application, or the said claims Nos. 17 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-17

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-17
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-17
Industrial applicability (IA)	Yes: Claims	1-16
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

10/574424
IAP20 Rec'd PCT/PTO 04 APR 2006
International application No.

PCT/IB2004/003373

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claim 17 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).

Re Item IV

Lack of unity of invention

1. The present application relates to the field of meningococcal vaccines. Meningococcal polysaccharide vaccines comprising conjugated polysaccharides from serogroups A, C, W135 and Y are described in the prior art (WO-02/058737). In view of the prior art, the underlying application attempts to solve the problem of providing further meningococcal vaccines. The following solutions are proposed in the claims:

Invention 1: Immunogenic composition comprising a conjugated capsular saccharide antigen of each serogroup C, W135 and Y, and one or more polypeptide antigens from serogroup B.

Invention 2: Immunogenic composition comprising a conjugated serogroup W135 capsular saccharide antigen and a conjugated H. influenza type b capsular saccharide antigen.

Due to the fact that meningococcal vaccines comprising conjugated capsular saccharides have already been described in the state of the art, in view of the essential difference in the solutions proposed to the problem posed, and since no other technical features can be distinguished, which, in the light of the prior art, could be regarded as special technical features, it is considered that neither the objective problem underlying the subjects of the claimed inventions, nor their solutions defined by the special technical features allow for a relationship to be established between the said inventions, which involves a single general inventive concept. In conclusion, the groups of claims are not linked by common or corresponding special technical features and define two different inventions not linked by a

single general inventive concept.

The application, hence does not meet the requirements of unity of invention as defined in Rules 13.1 and 13.2 PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: WO 02/058737 A (AVENTIS PASTEUR) 1 August 2002 (2002-08-01)
- D2: VEGA MASIGNANI ET AL.: "Vaccination against Neisseria meningitidis using three variants of the lipoprotein GNA1870" JOURNAL OF EXPERIMENTAL MEDICINE, vol. 197, no. 6, 17 March 2003 (2003-03-17), pages 789-799, XP002286107
- D3: MARIAGRAZIA PIZZA ET AL.: "Identification of vaccine candidates against serogroup B meningococcus by whole-genome sequencing" SCIENCE, vol. 287, 10 March 2000 (2000-03-10), pages 1816-1820, XP000914964
- D4: JEANNETTE ADU-BOBIE ET AL.: "Two years into reverse vaccinology" VACCINE, vol. 21, January 2003 (2003-01), pages 605-610, XP004401591
- D5: MARIROSA MORA ET AL.: "Reverse vaccinology" DRUG DISCOVERY TODAY, vol. 8, no. 10, May 2003 (2003-05), pages 459-464, XP002324779
- D6: WO 03/020756 A (CHIRON SPA) 13 March 2003 (2002-08-01)

1. Claims 1-17 are directed to an immunogenic composition comprising a conjugated capsular saccharide antigen of each serogroup C, W135 and Y, and one or more polypeptide antigens from serogroup B. Since such compositions have not been disclosed in the state of the art, claims 1-17 are novel in accordance to Article 33(2) PCT.

2. Document D1 discloses an immunological composition comprising two or more protein-polysaccharide conjugates from capsular polysaccharides of N. meningitidis serogroups A, C, W135 and Y (page 4, par. 21 - page 6, par. 30). Details of the vaccine formulation and

administration route are provided (page 6, par. 31 - page 8, par. 37). Document D1 formulates as well the broadly recognized problem that the serogroup B polysaccharide is poorly immunogenic (page 2, par. 9). In the light of the prior art, therefore, the problem to be solved consists in providing a meningococcal vaccine against serogroups A, C, W135, Y and B with an immunogenic component of serogroup B. The solution provided by the applicant consists in the use of polypeptide antigens from serogroup B. However, this solution has been already devised in D2, in an attempt of solving the same problem (page 790, col. left, pars. 2-3). D2 discloses an immunogenic composition against serogroup B comprising *N. meningitidis* GNA1870 lipoprotein (page 793, col. left, par. 2 - page 795, col. right, par. 2). The protein appears to be bactericidal against most strains (page 796, col. right, par. 2 - page 797, col. left, par. 1). Three variants are described which correspond with the protein designated in the application as '741' protein. It would be obvious for the skilled person to add the GNA1870 protein of D2 to the vaccine composition of D1 in order to solve the problem posed. Furthermore, documents D3, D4 and D5 describe a general method for identifying vaccine candidates against serogroup B *Meningococcus*, among which the Nada protein is cited (D4). Consequently, claims 1-8 and 10-17 do not involve an inventive step and do not comply with the requirements of Article 33(3) PCT.

3. Claim 9 refers to the composition comprising the particular polypeptides of SEQ ID Nos:2, 7 and 8. Document D6 discloses hybrid neisserial proteins among which SEQ ID Nos2, 7 and 8 are described. It is mentioned that the proteins can be used in immunogenic compositions and in combination with other antigens, such as a saccharide antigen from *N. meningitidis* serogroups A, C, W135 and/or Y (page 10, line 1 - page 11, line 3). It would be therefore obvious to the skilled person to provide such a composition as claimed in claim 9. Consequently, claim 9 does not involve an inventive step and does not comply with the requirements of Article 33(3) PCT.

4. For the assessment of the present claims 15 and 16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**WRITTEN OPINION OF THE
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AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/IB2004/003373

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
IB2004/000651	12/8/2004	30/1/2004	30/1/2003
IB2003/004848	22/4/2004	2/10/2003	11/10/2002
IB2004/000673	12/8/2004	30/1/2004	30/1/2003
IB03/02382	20/11/2003	14/5/2003	14/5/2002

Re Item VII

Certain defects in the international application

1. The vague and imprecise statement in the description on page 37, last paragraph implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them.

2. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D2-D6 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII

Certain observations on the international application

1. The internal designations for proteins used in claim 8 ('NadA', '741', '936', '953' and '287') are meaningless and do not convey any technical features to the subject-matter. A protein should be defined by its aminoacid sequence (Article 6 PCT).